REMARKS

The Claim Amendments

Claims 1, 8-10, and 26 are pending. Claims 2-7 and 11-25 have been canceled as drawn to a non-elected invention. Claim 1 has been amended to indicate that UP is uridine phosphorylase. Support for the amendment is found in the specification at, for example, page 2, lines 29-31. Claim 10 has been amended to indicate that PMO is phosphothioate morpholino oligomer. Support for the amendment is found in the specification at, for example, page 18, lines 15-16. New claim 26 has been added which recites "[t]he method of claim 8 wherein the nucleic acid modulator is an siRNA". Support for the new claim 26 is found in the specification at, for example, pages 18, line 24 to page 19, line 2, and pages 39-41.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections and are fully supported by the specification as filed. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application. The amendments add no new matter and applicants respectfully request their entry.

Claim Objections

Claims 1 and 8 were objected to because the abbreviated term "UP" was not described in either initial or subsequent occurrence in claims. Claim 1 has been amended to recite that "UP" is uridine phosphorylase.

35 U.S.C. § 103(a)

Claims 1 and 8-10 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over WO 03/052068 (Costa) in view of Liu et al, Cancer Research 58:5418-5424 (1998). Applicants respectfully traverse the rejection.

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The Office Action alleged that Costa et al. teach a method of identifying a candidate beta-catenin pathway modulating agent comprising providing a PMO antisense oligomer to an assay system and detecting the difference between the test sample and the control (reference) sample in the assay system . The Office stated that Costa et al. do not teach that UP is one of the beta-catenin modifier genes. The Office alleged that Liu et al. teach that human uridine phosphorylase activity is up-regulated in tumor tissues compared to normal tissues and suggest that blocking UP activity may provide strategies for treating tumors. The Office argued that since Costa et al. provided methodologies for identifying a beta-catenin modifier gene and since UP activity was known to be significantly elevated in tumor cells and therefore implicated in cell proliferation as taught by Liu et al. one would have necessarily identified UP as one of the beta-catenin modifier genes and therefore would have used a UP PMO antisense oligonucleotide in an assay system and verified that the UP PMO antisense oligonucleotide is a beta-catenin pathway modulating agent. The Office thus concludes that the claimed invention would have been *prima facie* obviousness.

Contrary to the Office's allegations, the teachings of Costa et al. and Liu et al, alone or in combination, do not render obvious the present invention. The instant claims are directed to a method of identifying a candidate beta-catenin pathway modulating agent comprising the steps of: (a) providing an assay system comprising a UP nucleic acid; (b) contacting the assay system with a candidate test agent; and (c) detecting a test agent-biased activity of the assay system. Thus, the present claims utilize an assay system comprising a UP nucleic acid to identify a candidate beta-catenin pathway modulating agent.

First, Applicants submit that one skilled in the art would not have been motivated to combine the teachings of Costa et al. and Liu et al. Second, Applicants submit that even if one would have been motivated to combine the teachings of Costa et al and Liu et al, the combined teachings would not have led to the presently claimed methods. Although Costa et al. identifies several nucleic acids (MBCAT genes) that can be used in an assay to identify a beta-catenin modulating agent, it fails to contemplate or suggest using a UP nucleic acid in such assay. Thus, one skilled in the art would not have been

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motivated to seek teachings related to UP gene, including the teachings of Liu et al. While the Office does not provide a reason that one skilled in the art would have specifically identified a UP nucleic acid out of all the other possible nucleic acid molecules for use in an assay to identify candidate beta-catenin modulating agents and also does not provide an explicit reason why one skilled in the art would have pursued the teachings of Liu et al, it seems to suggest that UP would have been a logical gene to pursue because UP was known to be involved in cell proliferation. However, there are hundreds of genes implicated in cell proliferation. In the absence of any teaching or suggestion to pursue the use of a UP nucleic acid, one skilled in the art would have had no reason to select a UP nucleic acid over the hundreds of other possible nucleic acid molecules and would have had no reason to seek the teachings of Liu et al.

Further, even if for the sake of argument, one would have been motivated to seek the teachings of Liu et al., the combined teachings of Costa et al and Liu et al. would not have led one skilled in the art to arrive at the presently claimed methods. Costa et al. describes methods of identifying a candidate beta-catenin pathway modulating agent utilizing an assay system comprising an MBCAT nucleic acid (see Table 1). Costa et al. makes no mention of UP gene and thus fails to teach or suggest a method of identifying a candidate beta-catenin pathway modulating agent using an assay system comprising a UP nucleic acid. Liu et al fails to cure the deficiencies of Costa et al. Liu et al. merely describes cloning UP gene and describes some of the characteristics of UP, including teaching that UPase activity is 2-3 fold higher in some tumors compared with normal tissue. Liu et al is not at all concerned with genes modulated by UP or with assays that could be used to identify such modulation. Further, Liu et al makes no mention whatsoever of beta-catenin and thus, like Costa et al., fails to recognize a connection between UP and beta-catenin. However, it is precisely the connection between UP and beta-catenin that is the crux of the presently claimed method. Given that neither Costa et al, nor Liu et al recognize a connection or nexus between UP and beta-catenin, the teachings of Costa et al and Liu et al, alone or in combination, fail to teach an assay wherein a UP nucleic acid can be used to identify a candidate beta-catenin modulating agent.

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Despite the complete lack of teaching of any connection between UP and beta-catenin and the lack of any suggestion whatsoever to use UP nucleic acid in an assay for identifying a candidate beta-catenin pathway modulator, the Office argued that one of ordinary skill in the art performing the method of Costa et al. would have necessarily identified UP as one of the beta-catenin modifier genes and therefore one skilled in the art would have used a UP PMO antisense oligonucleotide in an assay system to identify or verify that the UP PMO antisense oligonucleotide is indeed the beta-catenin pathway modulating agent. The Office then concluded that "[s]ince the knowledge and skills required to arrive at the claimed invention were within the technical grasp of one of ordinary skill in the art, and since Costa et al. provided the step-by-step guidelines for the claimed method (see claims 1 and 8-10 of Costa et al.), the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing." (Offfoce Action at page 5).

However, Applicants point out that Costa et al uses a different method of identifying beta-catenin pathway modulating agents (C. elegans system) than the method used in the instant application to identify UP as a beta-candidate pathway modulator (Drosophila melanogaster system). Thus, it is not clear that one of ordinary skill in the art performing the method of Costa et al. would have "necessarily identified UP as one of the beta-catenin modifier genes" as stated in the Office Action (page 4) and the Office has not presented any scientific evidence to support its bald assertion. Furthermore, as indicated in the MPEP at §§2143.01 and 2143.02, a reference containing enabling methodology (as the Office characterizes Costa et al.) is not sufficient to establish a *prima facie* case of obviousness. There must further be a suggestion to modify the prior art to produce the claimed invention and a suggestion that such modification would be successful. MPEP §2143.02.

Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness because it has failed to provide a motivation or reason that would have prompted one skilled in the art to modify the teachings of Costa et al to select a UP nucleic acid for use in the claimed assay. Prior to Applicants disclosure in the instant application there was simply no teaching or suggestion of the connection between the UP

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gene and the beta-catenin pathway. Thus, there was no teaching, suggestion, or motivation in Costa et al, Liu et al., or other known art to modify the teachings of Costa et al to select a UP nucleic acid out of the hundreds of other possible genes that could have been selected. Furthermore, in the absence of any teaching or suggestion of the connection between UP gene and beta-catenin, the results obtained in the instant application would not have been predictable to one of ordinary skill in the art. Thus, there would have been no reasonable expectation (prior to Applicants' instant disclosure) that UP could have successfully been used in an assay to identify a candidate beta-catenin modulating agent.

Accordingly, Applicant respectfully requests withdrawal of the 35 U.S.C. § 103(a) rejection.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the Examiner believes a teleconference will advance prosecution, she is encouraged to contact the undersigned as indicated below.

Respectfully submitted,
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